Hair Cells From Stem Cells

Drug Discovery & Development Staff

In a research area that will generate blockbuster profits if/when it pans out, a science team reported creating new hair cells from pluripotent stem cells in a recent issue of *PLOS* [1] *(Proceedings of the Library of Science) One*.

The team, led by the Sanford Burnham Medical Research Institute, got their results using two different kinds of cells: embryonic stem (ES) cells and induced pluripotent stem (iPS) cells. ES cells can form all body cells. IPS cells can, as well. The difference is iPS cells are derived from adult cells, not in vitro fertilization (IVF) clinic embryos. The clock is turned back on the adult cells, until they reach a pluripotent state like that of ES cells.

“The relative simplicity of the procedure to derive [dermal-papilla]-like cells was a pleasant surprise,” Sanford Burnham developmental biologist Alexey Terskikh told *Drug Discovery & Development*. Terskikh is senior author on the paper. “To the best of my knowledge, we are the first team to report the generation of hair inducing cells” from embryonic stem cells. “The most critical next step is to investigate whether this approach works in humans.”

The new approach

Terskikh's group believes their creation of neural crest cells from ES cells, which then formed dermal papilla cells, was a key step. Dermal papilla cells regulate hair-follicle formation and growth cycle. Limited adult dermal papilla (DP) cells do not work as hair transplants as they generally can't be obtained in the large amounts, and can quickly lose hair-follicle forming ability in culture.

But neural crest cells transiently arise from the dorsal neural tube during development, and give rise to many tissues at that time, including hair follicle cells. So Terskikh's group first worked on persuading their pluripotent cells to become neural crest cells. Human ES cells "have been directed [3] to various cell fates including hair follicle epidermal cells—keratinocytes; however, the derivation of DP cells have not been reported" from ES cells, the team wrote. "Here we describe for the first time the derivation of functional DP-like cells human embryonic stem cells."

The group reported their human ES-cell derived neural crest cells, cultured in serum, progressively acquired the markers of DP cells, and gave rise to cell populations with "robust" hair-inducing potential in mice. They speculated the superior hair-creation capacity of their pluripotent cell derived DPs to most reported adult DPs may have to do with the resemblance of their cells to embryonic or neonatal DP precursor cells.

The group also reported their cells are heterogeneous, a "mixed population" of neural-crest-derived cells that "contain DP-like cells with hair-inducing properties, but also might contain melanocyte- and keratinocyte-forming cells." Therefore, "further analysis…is needed to address this question."

The group also noted they had more success with human ES cells than with human IPS cells. They only achieved hair cells with one of three iPS cell lines. However, if many lines are used, hair cells should ultimately result, they wrote.

Overall, the group reported, "our results suggest that the intermediate step of hESC

differentiation into the NC [neural crest] lineage seems critical, skipping the NC induction results in a complete loss of hair-inducing activity." The group believes that directing human ES cells to neural crest cells "might limit the variety of mesenchymal cell types to the subset that is developmentally specified downstream from NC cells in skin (e.g. cephalic DP during development, melanocytes, cephalic bulge)." Resulting cultures become "enriched in hair-inducing DP-like cells using relatively common mesenchymal-enriching conditions, such as differentiation in serum containing medium and selection for the adherent cell types."

The group said adult skin-derived precursors [4] have been found in the past to be "highly potent in hair induction, but progressive loss" of those cells during aging "might hamper the process of isolation" of those cells.

In 2013, a Columbia University and Durham University team reported pairing up to generate significant [5] hair growth, for the first time, from adult DP cells using unique 3-D cultures. Results varied between donor cells, but those groups reported they were perfecting that approach.

Links:
[1] http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0116892
[2] http://register.rdmag.com/rd100-analytical/
[3] http://onlinelibrary.wiley.com/doi/10.1634/stemcells.2007-0501/abstract;jsessionid=DB8620738FA828A9CA89CC311133385F.f04t04
[4] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2828150/
[5] http://www.biosciencetechnology.com/articles/2013/11/breakthrough-human-hair-growth-%E2%80%98tantalizes%E2%80%99-experts